Strategies to Reduce Antimicrobial Resistance in Food Animal Agriculture

Summary

Limiting availability of antimicrobials, enhanced surveillance, and on-farm interventions (including prudent antimicrobial use and management practices) have been proposed as key strategies to reduce antimicrobial resistance in food animal agriculture. Improved, rapid diagnostic methods and accelerated development and approval of new antimicrobial drugs can also play an important role in preventing and controlling antimicrobial resistance. This report describes the essential characteristics of a surveillance system for antimicrobial resistance and briefly reviews recently organized surveillance systems in the U.S., France, and Sweden. In addition, management practices that can decrease the need for antimicrobial use on the farm are explored. Examples of management practices that decrease the need for antimicrobials are the use of vaccines, probiotics, immune enhancers, good husbandry practices, and biosecurity. According to data from the USDA's National Animal Health Monitoring System (NAHMS), enhanced use of health management practices could reduce the requirements for antimicrobial drugs that are used for therapeutic purposes on U.S. swine, dairy, and beef operations. Some specific results of NAHMS' health management data were: (1) Only 32% of calves received the recommended volume of colostrum during the first feeding. (2) The immunoglobulin concentration was less than ideal in approximately 67% of the 2,177 dairy calves sampled. (3) Proper protection against respiratory pathogens may have been inadequate in as many as 86% of beef calves in the U.S. at the time of sale in 1997, based on the frequency of vaccination. Educating animal producers and veterinarians concerning these strategies to prevent and control antimicrobial resistance is an essential component for the strategies to be effective.

Introduction

Strategies to identify and reduce antimicrobial resistance in food animal agriculture should include interventions at all levels, from global to national and local, including the individual farm and animal. National laws and regulations pertaining to antimicrobial licensure and compliance can effectively limit availability to antimicrobials (WHO, 1997). National laws and regulations can also be used to stimulate new antimicrobial drug discovery and to accelerate new drug approval. Monitoring and surveillance of antimicrobial resistance in food animals is an intervention activity that should operate at all levels, global, national and local. Surveillance needs to track both resistant organisms and antimicrobial use. A surveillance system to monitor the prevalence of resistant organisms should provide the necessary information to determine the magnitude of the problem and evaluate the impact of interventions aimed at decreasing resistance. A database system to collect information on amount and methods of antimicrobial use in food animal agriculture is also needed. Ideally, the information on antimicrobial use should be able to relate back to the information on resistance. It is important that these database systems be able to track trends over time and can also harmonize with both human and international surveillance systems.

In addition to limiting availability to antibiotics, and monitoring and surveillance programs, on-farm interventions at the local level may reduce the risk of antimicrobial resistance. On farm interventions include prudent use of antimicrobials and implementation of management practices which decrease the need for antimicrobials. Prudent use of antimicrobials is defined as use in a manner that promotes their effectiveness yet minimizes bacterial resistance development (Apley et al., 1998). Development of new diagnostic methods to quickly differentiate viral from bacteria infections, identify the specific viral or bacterial infection, and determine drug susceptibility of the organism, can facilitate prudent use of antimicrobials (Huovinen, 1998). Examples of management practices that decrease the need for antimicrobials are the use of vaccines, probiotics, immune enhancers, good husbandry practices, and biosecurity.

Limiting Availability to Antimicrobials

Recent controversies surrounding the approval of fluoroquinolones in food animals has brought the process of antimicrobial drug approval for food animals under scrutiny. In January, 1999, the FDA published in the Federal Register a discussion paper titled "A Proposed Framework for Evaluating and Assuring the Human Safety of the Microbial Effects of Antimicrobial New Animal Drugs Intended for Use in Food-Producing Animals". The proposed regulations are aimed at reducing antimicrobial resistance development in zoonotic, foodborne pathogens. The Framework outlines the following five components of how to evaluate and minimize the potential human health effects of uses of antimicrobial drugs in food-producing animals:

1) assess the effect of proposed uses on human pathogen load;
2) assess the safety of proposed animal uses of drugs according to their (or related drugs) importance in human medicine and the potential human exposure to resistant bacteria acquired from food-producing animals that are human pathogens or that can transfer their resistance to human pathogens;
3) assess pre-approval data showing that the level of resistance transfer from proposed uses of drugs, if any, will be safe;
4) establish "resistance" and "monitoring" thresholds to ensure that approved uses do not result in resistance development in animals or transfer to humans above the established levels; and
5) establish post-approval studies and monitoring.

Surveillance of Antimicrobial Resistance

The aims of a resistance monitoring program are described in the World Health Organization's report on the "Medical Impact of the Use of Antimicrobials in Food Animals" (WHO, 1997). A resistance monitoring program should gather information to promote prudent and judicious use of antimicrobials in livestock production, enable informed decision-making by national regulatory institutions, guide prescription practice, encourage standardization of laboratory techniques for monitoring, identify areas for more detailed investigation and promote collaboration.

The following characteristics of an ideal surveillance system are from the Workshop Report on Antimicrobial Resistance: Issues and Options, Institute of Medicine, 1998. An ideal system should:

1) be prospective, active, timely, and affordable;

2) provide accurate incidence rates and prevalence, which would in turn require both numerator and denominator information (e.g., the number of isolates tested and the number of resistant isolates), as well as a mechanism to permit exclusion of repeat isolates from the data pool;
3) include information that identifies organisms causing infection and those involved in colonization (i.e., the ability of a bacterium to remain at a particular site and multiply there);
4) gather data so as to permit categorization by region and locality, as well as to discriminate between animal species and clinically ill versus healthy animals;
5) gather information on antimicrobial use and treatment outcomes, especially treatment failure (the outcome of resistance);
6) be able to detect new resistance markers and therefore be dependent on standardized and reliable laboratory techniques, uniform criteria for determining resistance, appropriate specimens for culture, and adequate microbiologic validation;
7) be a national network representing all regions;
8) computerize all participating laboratories, regularly collect electronic data, process and report in ongoing fashion, and integrate all databases at the national level;
9) make surveillance data available to practitioners at the appropriate regional and local levels so that problems at these levels could be managed appropriately.

The Current U.S. Surveillance System for Antimicrobial Resistance in Animals

The current U.S. surveillance system for monitoring antimicrobial resistance of enteric bacteria in animals and humans is called the NARMS-EB (National Antimicrobial Resistance Monitoring System - Enteric Bacteria). The goals and objectives of the NARMS-EB monitoring program are to:

1) provide descriptive data on the extent and temporal trends of antimicrobial susceptibility in *Salmonella* and other enteric organisms from animal and human populations;
2) facilitate the identification of resistance in animals as it arises;
3) provide timely information to veterinarians and physicians;
4) prolong the life span of approved drugs by promoting the prudent and judicious use of antimicrobics; and
5) identify areas for more detailed investigation.

Monitoring is currently targeted to *Salmonella spp*., *Campylobacter*, and *E. coli*. *Salmonella* isolates are collected from multiple sources: (1) clinical isolates submitted to the National Veterinary Services Laboratories from around the country, (2) isolates collected as part of NAHMS periodic national surveys, (3) isolates from other epidemiological studies, and (4) all *Salmonella* isolates from slaughter samples around the country. Isolates from three diagnostic laboratories, one each in Washington, California, and New York were added to NARMS-EB in 1998. Isolates are collected from the various sources mentioned above and susceptibility testing is then conducted at a central location, the USDA:ARS Richard Russell Research Center in Athens, GA. The USDA agencies involved in NARMS are APHIS, ARS and FSIS.

Surveillance of Antimicrobial Use in Animals

In the U.S., detailed records are not kept at point-of-sale for animal antimicrobial use, unlike for human antimicrobial use. Producers can obtain certain antimicrobials over the counter at farm supply retail outlets, and veterinarians most commonly obtain antimicrobials from a pharmaceutical firm representative. Information on sales from the pharmaceutical industry is mostly proprietary. Therefore, there is a significant lack of detailed information on the amount, potency and characteristics of antimicrobial use in animal agriculture. Such detailed information is a critical component in evaluating the impact of antimicrobial use on antimicrobial resistance.

Veterinary Services' NAHMS program can play an important role in obtaining information on antimicrobial use on the farm with the cooperation of producers. Future objectives for NAHMS surveys can include collecting information on antibiotic use practices. Information on which antibiotics are used, when, how, and under what guidance, could be obtained and national estimates calculated. In addition, if future NAHMS surveys will be able to link resistant isolates with use of antibiotics on a specific operation, risk factors for antibiotic resistance could be evaluated.

Future Goals for Surveillance in the U.S.

The current U.S. Surveillance system for monitoring antimicrobial resistance in animals has a national focus, however it does not have the ability to produce data on antimicrobial resistance at the local level, or the resources to examine more than a few pathogens. If it is important to have more locality-specific information, perhaps for specific species of animals and representing additional genera of bacteria, several avenues are available to gather such data. First, the existing system could be expanded to incorporate additional clinical isolates from diagnostic laboratories. Second, passive monitoring of clinical isolate resistance patterns could be implemented if a private sector company were to implement a service to collate data on veterinary isolate resistance patterns such as is available for human isolates. Third, another entity, perhaps public or from academia, could initiate a system to collate data on resistance profiles of animal isolates from diagnostic laboratories. The NAHMS program has a history of working with diagnostic laboratories in the past to collate data on accessions and diagnoses. Thus NAHMS may be an appropriate organization to provide leadership for the surveillance system should the third approach be appropriate (Personal communication, David A. Dargatz, USDA/APHIS/VS, 1999). Regardless of how the data are generated and collated it will be imperative that they be channeled into a single system, analyzed and interpreted and that feedback be provided to diagnostic laboratories, and health care providers (human and animal) in order to facilitate prudent antimicrobial use decisions.

Before a new system based on resistance data from veterinary diagnostic laboratories can be initiated, standardization of resistance testing methods among laboratories must be assessed. The USDA/APHIS/VS Centers for Epidemiology and Animal Health (CEAH) is planning a survey of diagnostic laboratories to collect data on the resistance testing methodologies in use and to determine how the results of testing are being stored (Personal communication, David A. Dargatz, USDA/APHIS/VS, 1999). The results of this survey will provide an assessment of current feasibility and any changes which will be required, to improve standardization and facilitate data aggregation, before this type of surveillance system can be implemented.

Antimicrobial Resistance Surveillance Systems - International Perspective

Information from surveillance systems for antimicrobial resistance is necessary to evaluate even superficially the validity of reports of increasing prevalence of resistance to antimicrobial drugs. Surveillance systems explicitly for antimicrobial resistance will provide the best estimates of the prevalence of resistance. Such surveillance systems have been organized in France, Sweden, and as described above, in the United States.

<u>France:</u> The primary focus of systems that have been described in France is zoonotic salmonellosis. Since 1978, the National Veterinary and Food Research Centre (CNEVA) through the CNEVA-Paris and the CNEVA-Lyon has been monitoring the antibiotic resistance of *Salmonella* and observing the spread of multiresistant isolates of serotypes isolated from animals, especially from cattle and poultry operations, and from their environments (Brisabois et al., 1997). Isolates associated with epidemiological information are collected from a network of nearly 200 veterinary or food hygiene laboratories. An inventory of *Salmonella* serotypes and antibiotic resistance has been published every two years for more than twenty years. For epidemiological analysis of the serotypes and antibiotic resistance patterns, the isolates are subdivided according to their source:

- isolates from animal samples,
- isolates from food hygiene samples, including feedstuffs,
- isolates from environments, including animal production environments and the natural ecosystem.

During 1994 and 1995, 25,220 *Salmonella* isolates were collected by the CNEVA-Paris, and 15,878 were tested for antimicrobial susceptibility (Brisabois et al., 1997). Among the 25,220 isolates, 7,691 (30.5%) were from animals, 12,220 (48.5%) from food hygiene and 5,309 (21%) from environments.

Since 1982, the RESABO Network, a national veterinary network of 40 regional veterinary diagnostic laboratories, has monitored resistance to antimicrobials by common pathogenic bacteria from cattle, including *Salmonella* (Brisabois et al., 1997). Standardized diagnostic methods are used by the RESABO Network, which is managed by a central reference laboratory (CNEVA-Lyon). The RESABO network collects current data on antimicrobial resistance by veterinary isolates and analyzes isolates for specific mechanisms of resistance to antibiotics.

<u>Sweden</u>: Antibiotic resistance of *Salmonella* isolated from animals in Sweden has been surveilled since 1976, in accordance with WHO recommendations (Franklin, 1997). *Salmonella*, mostly *S.* Dublin or *S.* Typhimurium, are only sporadically isolated from production animals. Thus, surveillance in Sweden is primarily for purposes of human health.

Plans to Enhance Surveillance Systems for Antimicrobial Resistance In Europe

A comprehensive study of the prevalence of *Enterococcus faecium* resistance to avoparacin found the prevalence to be 59% in broiler chickens, 29% in pigs, and 0% in cattle (DIARMRP). Vancomycin-resistant enterococci (VRE), usually of *E. faecium*, can be resistant to numerous antibacterials. It has been suggested that animals may be a source of human infections (Bates et al., 1994). Thus, the use of avoparcin in animals has gained attention. The apparent link between avoparcin use in animals and the occurrence of vancomycin resistant *E. faecium* in pigs and poultry was highlighted by the Danish Veterinary Laboratory (Anonymous, 1995a). The EU SCAN Committee (i.e., Scientific Committee for Animal Nutrition) concluded that there was insufficient evidence to conclusively link avoparcin therapy in animals and VRE in humans. Nevertheless, the EU Commission suspended sales of avoparcin in April 1997 and requested:

1) data on antimicrobial resistance, especially due to glycopeptides.
2) a surveillance program for antimicrobial resistance in animals.

Consequently, a new surveillance system involving the United Kingdom, Spain, France, the Netherlands, Denmark and Sweden is being developed specifically for *E. faecium*. Samples from pigs and poultry will be tested for resistance to avoparcin, avilamycin, virginiamycin, flavomycin, tylosin/spiramycin, and bacitracin.

This surveillance program is expected to provide information on the susceptibility of isolates of *E. faecium* from European countries with a variety of husbandry systems, climates and policies related to feed additives. The program is not in itself expected to answer the crucial question regarding potential risk to humans, but it is expected to be of great interest in association with other data on transfer of resistance between species.

On Farm Interventions

Improving prudent use of antimicrobials

The primary responsibility for improving prudent use lies with the veterinary organizations such as the American Veterinary Medical Association (AVMA), American Association of Bovine Practitioners (AABP), and the American Association of Swine Practitioners (AASP). These organizations can provide guidelines aimed at reducing unnecessary use and promoting use which will mimimize antimicrobial resistance and maximize effectiveness of antimicrobials. In November 1998, the AVMA Executive Board approved a position statement and principles for judicious therapeutic antimicrobial use by veterinarians (Anonymous b, 1999).

Research into specific dose/duration regimens for specific antibiotics, rotating choices of antibiotics periodically and using combinations of therapy, and their impact on resistance development is needed. The private and university sectors need to be involved in this type of research. Clinical trials are needed to examine the effects of long-term, low-level antibiotic use, prophylactic use, and therapeutic use on antimicrobial resistance development. A monitoring program which can guide veterinary selection of appropriate antimicrobials based on regional/local trends in resistance is also needed. Information from these studies should feed back into prudent use guidelines.

Veterinary Services can assist prudent use efforts by characterizing current use methods, identifying areas where change is needed, monitoring progress through recurring surveys, and monitoring the success of education programs. Veterinary Services can also take a more active role in education. Veterinary Services already collects, analyzes and interprets data related to animal health and the production of livestock. In order to maximize the impact of this research, Veterinary Services needs to become more involved in educating producers and practitioners concerning the findings.

Management Practices That Decrease the Need for Antimicrobials

Conceptual shifts in thinking are needed to address the problem of antimicrobial resistance. One potential shift in thinking is to better understand and actively manage the microbial ecology of the farm, promoting and protecting the "good" microorganisms, and minimizing the "bad " microorganisms. Antimicrobials would then be used with a narrow focus only when needed and efforts would be made following antimicrobial therapy to restore a healthy, susceptible, microbial flora. Feedstuffs and management practices which promote a healthy microbial flora and a healthy immune system would be a priority.

Veterinary Services can play an important role in identifying management practices which promote animal health and productivity while minimizing antimicrobial use. NAHMS surveys can identify operations with low levels of resistance and identify which management practices are associated with low levels of resistance. Increasing use of vaccines has been proposed as a method to decrease antimicrobial use. This will require the widespread availability of highly efficacious vaccines that are easy to give at a reasonable cost. For many of the currently available vaccines, one or more of these criteria are perceived to be lacking. The Agricultural Research Service (ARS) can assist in this effort by conducting initial development of new vaccines or by conducting studies which show the cost effectiveness of existing vaccines. Development of vaccines is also a role of the biologics industry.

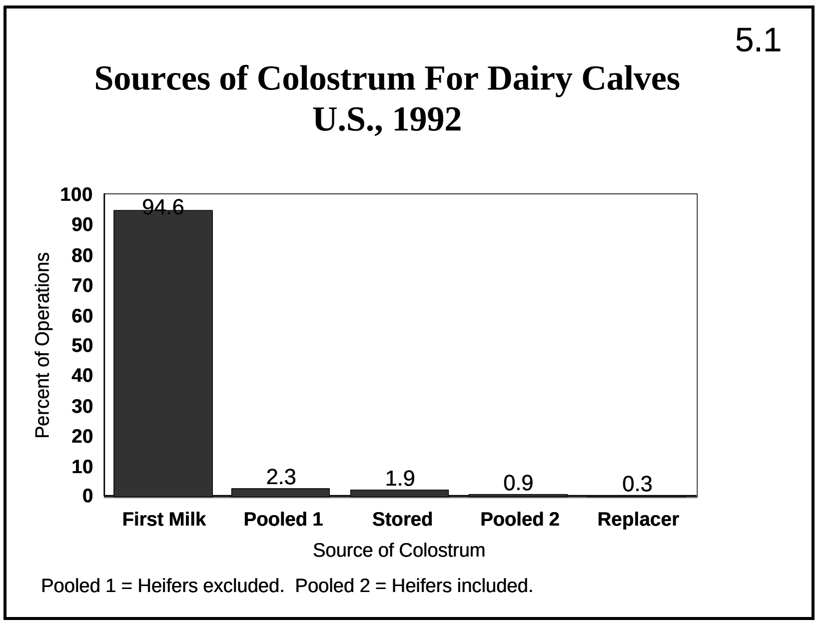
Development and use of immune modulators may help to reduce the need for antimicrobials. Attention to proper nutrition and adequacy of trace minerals in the diet are also key to an effective immune response in livestock. Research and development of probiotics, also known as competitive inhibitors, is being conducted by ARS. Research on cattle and swine probiotic products is currently underway at the ARS station in Texas. Several examples of potentially novel alternatives to using antimicrobials as growth promotants or prophylactics are currently under research/development by universities or private industry. These examples include: (1) avian antibodies for the prevention of *E. coli* infection in piglets and calves and for growth promotion in poultry and swine (Pimentel, 1999); (2) seaweed (*Ascophyllum nodosum*) meal to enhance immunity and for growth promotion in cattle, and (3) vitamin E supplementation in broiler diets to improve performance (Chung and Boren, 1999).

The application of more stringent biosecurity practices on operations, such as when new animals are introduced, may eliminate or reduce the risk of introduction of diseases that could require antimicrobial therapy. These practices may include: only buying animals from herds with known high health status; pre-arrival testing; and use of quarantine facilities. Practices to reduce feed and water contamination can also reduce disease risk.

Disease Prevention and Control Management Practices in the U.S.

Passive Immunity

Management factors that lead to inadequate natural and artificial immunity in animals may increase the demand for antimicrobial drugs on livestock operations. Colostrum is a newly born calf's most valuable source of protection against the early onset of disease. The duration of these protective antibodies in the serum of calves can be weeks to months. Results of the NAHMS

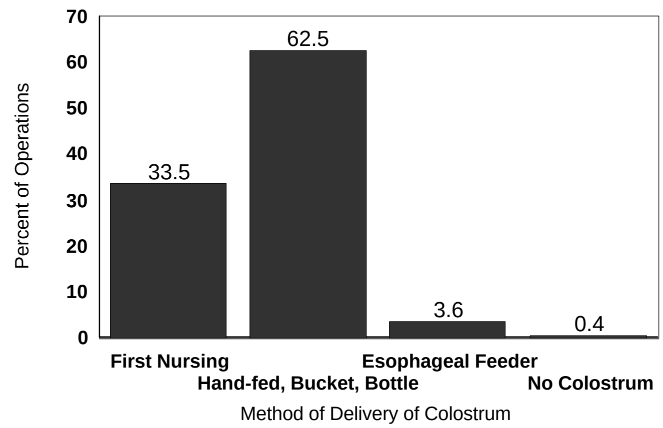


1992 National Dairy Heifer Evaluation Project (NDHEP) showed that calves on 95% of U.S. operations receive colostrum from their dam's first milking (USDA/APHIS/VS, 1993b) **(Figure 5.1)**. Calves on nearly two-thirds of the operations were fed colostrum from a bucket, bottle, or esophageal feeder, all of which provide some assurance of the volume of colostrum being ingested by the calves **(Figure 5.2)** . The remaining one-third of the calves received colostrum via first nursing, or did not receive colostrum.

Four quarts of colostrum is the recommended volume for the first feeding to prevent failure of passive transfer (Roussel et al., 1999). Only 32% of calves received 4 quarts or more during the first feeding **(Figure 5.3)**. The immunoglobulin concentrations were less than 1,000 mg per dl in more than 40% of the 2,177 dairy calves sampled, and the concentration was unmeasureable (i.e. less than 620 mg per dl) in more than 27% of the calves **(Figure 5.4).** Twenty-two percent of all dairy calf deaths may be prevented by ensuring that calves consume adequate volumes of colostrum (USDA/APHIS/VS, 1993c). The volume of colostrum consumed by beef calves is

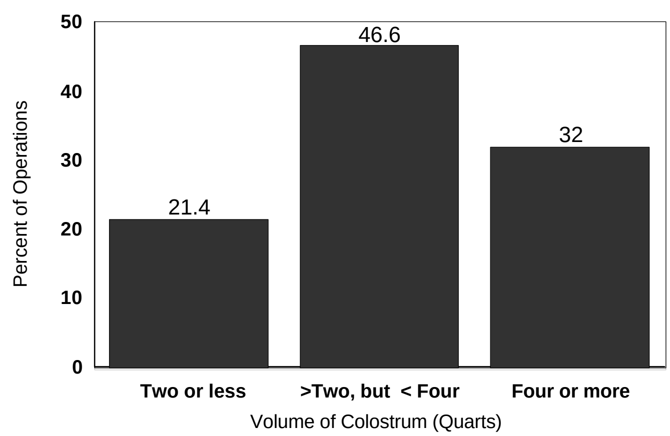
5.2

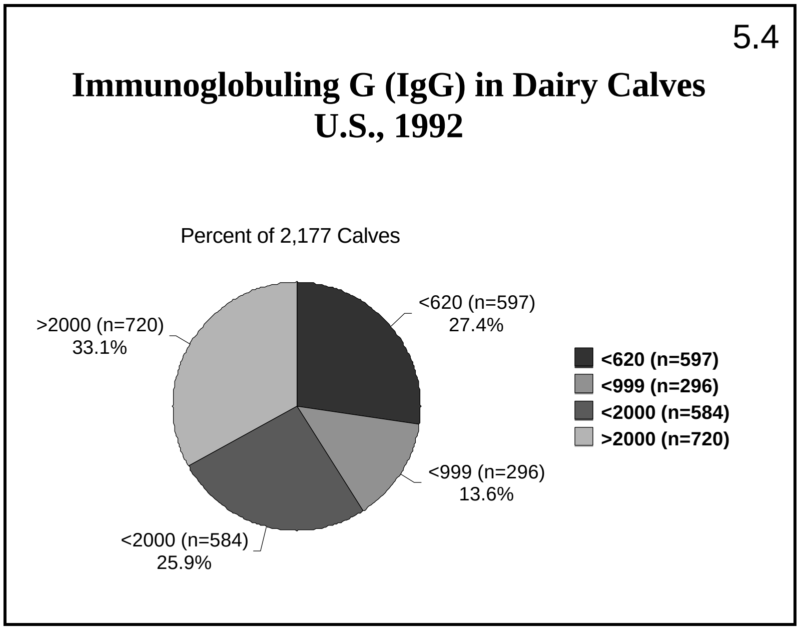
First Feeding Of Colostrum To Dairy Heifers
U.S., 1996



5.3

Volume of Colostrum Fed Manually To Dairy Heifers
U.S., 1996





more difficult to measure than in dairy calves. However, a smaller volume is required to provide passive immunity in beef calves versus dairy calves, partly because the immunoglobulin concentration is greater in colostrum from beef cows (Roussel et al., 1999).

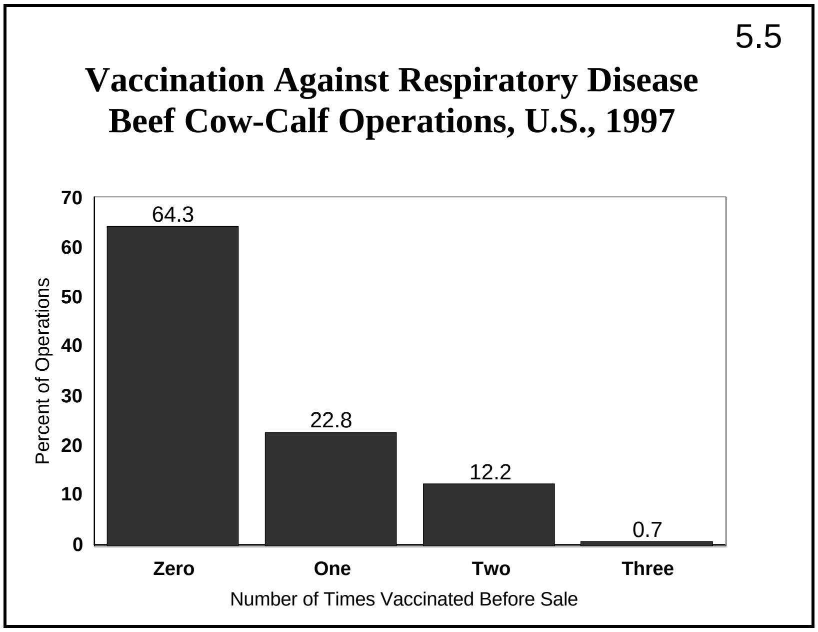
Increased use of antimicrobial drugs may be essential to protect dairy and beef calves with failure of passive transfer from bacterial infections, or from viral infections that are complicated by bacterial infections. Providing calves with adequate passive protection may reduce these deaths and decrease the demand for prophylactic and therapeutic antibiotics.

Active Immunity

Vaccination Frequency

Efficacious vaccines can provide calves with artificial immunity, if natural immunity has not been achieved via consumption of colostrum (Wren, 1997; Roth, 1997) . More than 64% of beef calves were not vaccinated against respiratory disease prior to sale in 1997, and 22% were vaccinated only once (USDA/APHIS/VS, 1998) **(Figure 5.5)**. Frequently two injections of a vaccine are recommended to stimulate the primary and anamnestic responses, both of which are essential for optimal immunoprophylaxis against disease. Thus, protection against respiratory pathogens at the time of sale may have been inadequate in as many as 86% of beef calves in the U.S. in 1997, based on the frequency of vaccination. Infectious bovine rhinotracheitis (IBR), bovine viral diarrhea (BVD) virus, and bovine respiratory syncytial virus (BRSV) are three pathogens associated commonly with the bovine respiratory disease complex (BRDC). Killed and modified-live versions of vaccines for these pathogens are available. Although revaccination within 60 days of the first vaccine is recommended by the manufacturers, only 28% to 29% of those producers who vaccinated against BRDC followed the manufacturers' recommendations.

Vaccination Timing



The effectiveness of vaccines is determined in part by the interval between vaccinations, in addition to the number of vaccines as described above. For operations that vaccinated calves for respiratory disease at least once, 36% vaccinated the calves at weaning, and 20% vaccinated after weaning, but prior to selling the calves. The stress and possible immune suppression that are coincident with weaning may sufficiently decrease the immunologic response to the vaccine to the point of being effective only marginally. Increased use of antimicrobial drugs may become essential to prevent or control what could be vaccine-preventable respiratory infections in beef calves prior to weaning.

Biosecurity

Minimizing the risk of introducing disease to an operation should be a relentless goal of all herd health programs. General principles of biosecurity such as restricted access of non-farm personnel, internal (versus external or purchased) replacements of livestock, and animal quarantine and/or isolation can be used to prevent the introduction of infectious diseases to farms. These practices can be used also to prevent animal-to-animal transmission of diseases, after a disease has been introduced to the farm. Both of these practices could contribute subsequently to the decrease in antimicrobial use (Sischo, 1997; Wren, 1998). Biosecurity practices on U.S. swine, dairy, and cow-calf operations were a part of the NAHMS studies between 1990 and 1997.

Swine Biosecurity

Slightly more than 40% of swine operations “restricted entry” into their operations to their employees only (USDA/APHIS/VS, 1992; USDA/APHIS/VS, 1995). Feed delivery personnel, livestock haulers, and other visitors were among non-employees who were permitted on those operations with “non-restricted entry”. Livestock haulers have been shown to be a potential risk factor for inter-farm transmission of pseudorabies virus and could serve as a vehicle for other infectious agents for which antibiotics would be an appropriate intervention (Austin et al., 1993). Less than 2.0% of all U.S. swine operations required a footbath and less than 1.0% required a shower of feed delivery personnel and livestock haulers before they were permitted on the operation. Less than 3.0% of all U.S. swine operations required a footbath and less than 1.0% required a shower of visitors other than feed delivery personnel and livestock haulers, before they were permitted on the operation. Breeding females were never quarantined by 50% of operations, breeding males were never quarantined by 36%, and feeder pigs were never quarantined by 72% of the operations. More than 50% of the operations did not screen the health of breeding females and breeding males using biological specimens (e.g., blood) before admitting these animals to the operation. For feeder pigs, this percentage was 81%.

Dairy Biosecurity

According to the NDHEP, 46% of U.S. dairy operations brought cattle onto their operations during the 12 months prior to this 1991 survey (USDA/APHIS/VS, 1993a). Dairy cattle at virtually every stage of production (e.g., calves, dry cows) were brought onto the operations. More than 25% of the operations brought on either lactating cows and/or heifers. More operations quarantined calves and young heifers than other older cattle, but the operations that quarantined calves and young heifers represented only 27% of all operations that brought on calves and young heifers. In general, quarantines were used infrequently on dairy operations. Only 5% of the operations washed the cow's udder prior to birth of the calf, and only 46% of the operations applied an antiseptic to the navels of newborn calves. Feeding utensils were shared by calves on 84% of all operations, but the utensils were washed and/or sanitized from one calf to the next on 17.9% of the operations only. Close physical association between young and adult stock may promote transmission of some infectious diseases, e.g., paratuberculosis (Bungert 1997; Wren 1998). Young, preweaned calves had close physical contact with older, weaned calves on nearly 32% of the operations.

Beef Biosecurity

Brucellosis, bovine viral diarrhea (BVD), infectious bovine rhinotracheitis (IBR), and leptospirosis are infectious diseases that may cause significant reproductive losses in herds. Vaccines may be used to prevent these infections in animals currently in residence on the farm (Wren 1997). Vaccines may be used also as a biosecurity tool to reduce the risk of introducing the infections via herd additions. Less than one-third of producers that brought cattle onto U.S. beef operations required vaccination of females for brucellosis (USDA/APHIS/VS, 1998). Only 13% of operations adding new animals required vaccination for either BVD, IBR, or leptospirosis. Newly admitted animals that have not been vaccinated may be carriers of these pathogens, unless diagnostic tests have been used to confirm that they are free of disease. Less than one-third of producers that brought cattle onto U.S. beef operations required that the animals be tested for brucellosis prior to being admitted to the operation (USDA/APHIS/VS, 1998). No more than 4% of the operations that admitted new animals required that they be tested for BVD, Johne's disease, or bovine tuberculosis (TB) prior to being admitted to the operation. While the percentage for brucellosis is significantly higher than for BVD, Johne's, and TB, requesting diagnostic tests to minimize the risk of disease transmission may not be the motive for this difference. Rather, the difference may be due to regulations related to interstate movement of animals**.**

Minimizing Antimicrobial Use - International Perspective

Although there has been general consensus that the prevalence of resistance is correlated closely with the prevalence of antimicrobial drug use, the epidemiologic evidence to support this belief has been lacking, until recently. According to the Finnish Study Group for Antimicrobial Resistance, the prevalence of resistance of group A streptococci to erythromycin increased from 5% in 1988 to 13% in 1990 (Seppala et al., 1997). This increase was correlated with a three-fold increase in consumption of erythromycin from 1985 to 1988. A nation-wide reduction in the consumption of erythromycin from 1991 to 1996 was followed by a decrease in the prevalence of erythromycin resistance from 16.5% in 1992 to 8.6% in 1996. It has been suggested that the correlation between the prevalence of resistance and erythromycin consumption provides a scientific basis for a permanent reduction in antimicrobial drug use in food animal production (Blaha, 1997).

There is substantial anecdotal evidence antimicrobial drug use is lower on healthy operations (Blaha 1997). Management practices that tend to be associated with the medical (versus financial) health of a swine operation are: (1) source herds, (2) all-in all-out pig flow, (3) group farrowing and transfer of closed groups, (4) matching based on health status, (5) specific pathogen free (SPF) animals, (6) and segregated early weaning (SEW). There is some evidence that SEW significantly reduces antibiotic use. A pork production system in which the objective is to completely eliminate antibiotics has been created by one Finnish food company. Consumption of antibiotics has been reduced by 70%, and more than 90% of the pigs are not exposed to antibiotics (Tuovinen et al., 1997).

Epidemiological studies (e.g., the NAHMS program) could play a significant role in verifying these anecdotal reports that specific management practices may significantly reduce antimicrobial use on farms (Blaha 1997). In addition to the management practices mentioned above, veterinary hygienic measures, or good production practices (GMPs), represent “. . . the most important . . .” barrier to epidemics of veterinary infectious diseases. GMPs include proper: (1) hygiene of feed and water, (2) hygiene of air and climate, (3) husbandry and technology, (4) disposal of feces and sewage, (5) protection of the production unit against contamination from the environment, (6) cleaning and disinfection, and (7) all-in all-out systems (Martin, 1997).

Ban of Antibiotic Growth Promoters in Sweden

The total use of antibacterials in Sweden increased from 41.3 to 50.6 tons from 1980 to 1984 (Wierup, 1997). Requirements for a veterinary prescription for all antibacterials was introduced in 1986. Subsequently, the total use of antibacterials decreased by 49% from 50.6 tons in 1984 to 24.8 tons in 1986. By 1996, consumption of the active ingredients had decreased by 55% from the pre-ban (i.e., 1985) levels of consumption.

Is antimicrobial-free livestock production possible? Antibiotics for growth-promoting purposes have been banned in Sweden starting in 1986 (Wierup, 1997). Immediate attempts to improve the animal production environment were made in connection with this ban. A national standard for environmental improvement was created by poultry producers, and this standard became a target for which all poultry production units were to strive. Virginiamycin was used commonly prior to the 1986 ban on using this drug to prevent necrotic enteritis. Its use was continued during the transition period immediately after the ban (i.e., through 1987), suggesting the AGP ban in Sweden actually began in 1988, not 1986 (Wierup, 1997). Phenoxymethyl penicillin, an alternative to virginiamycin, was used first in 1987. The amount of active antibiotic ingredients in two commonly used antibiotics, virginiamycin and phenoxymethyl penicillin, decreased from 1,818 kg in 1987 (virginiamycin) to 100 kg in 1988 (phenoxymethyl penicillin). Since 1995, virtually no antibiotics have been used in Sweden against necrotic enteritis in poultry.

Because antibiotics are effective growth promoters, it can be hypothesized that a ban on antibiotics would lead to decreased productivity (e.g., reduced growth rates). Two negative effects on productivity of the Swedish ban in “1986” were: (1) increased the age-to-30 kg. bodyweight by 2.0 days in pigs, (2) increased problems with necrotic enteritis in broilers, initially. Three un-altered effects of the Swedish ban in “1986” were: (1) did not decrease egg production in layers, (2) did not decrease growth rate in turkeys, (3) no reports of decreased productivity in specialized beef production. In conclusion, the Swedish Animal Health Service concluded that a ban on growth promoters provides evidence that poultry, calves, and pigs can be reared without continuous use of growth promoters, if the benefits of other production practices such as hygiene are maximized (Wierup, 1997). If the production data reported here were collected prior to 1988, they should be interpreted cautiously, since the true ban on all AGPs did not begin until 1988.

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